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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,700	GRAVETT, DAVID M.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-98* is/are pending in the application.

4a) Of the above claim(s) *2,4-7,13,16,33,36,37,63-65 and 68-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,8-12,14-15, 17-32, 34-35, 38-64, 66-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-98 are pending.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Election/Restrictions

Applicant's election of Group I in the reply filed on January 25 2008 is acknowledged. Applicant has elected for initial examination poly(ethylene oxide) as block X, poly-DL-lactide-co-glycolide (PDLLA) as block Y, naturally occurring amino acid and antimicrotubule drug. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-98 are pending in the application. Claims 2, 4-6, 33, 65, 68-98 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 7, 13, 16, and 36-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Accordingly, claims 1, 3, 8-12, 14-15, 17-32, 34-35, 38-64, and 66-67 are being examined on the merits herein.

Abstract

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because it contains legal phraseology such as comprising in line 2 of the abstract. Correction is required. See MPEP § 608.01(b).

Specification

The use of the trademark TAXOL® and TAXOTERE® (page 28, line 18) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 8-12, 14-15, 17-32, 34-35, 44-48, 52-53, 55, and 66-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (US Patent 6322805) in view of Park et al. (US PGPUB no. 20030031715).

Applicant Claims

Applicant claims a composition comprising a micelle-forming biocompatible diblock copolymer, an amino acid, and a hydrophobic drug. The composition forms a micellar solution in water.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Kim et al. is directed to a biodegradable polymeric micelle-type drug composition. The polymer material is a block copolymer prepared by combining a biodegradable hydrophobic polymer and a hydrophilic polymer. The hydrophobic polymers include poly(lactic-co-glycolic acid) and the hydrophilic polymer is poly(alkylene oxide) (column 4, lines 27-32). Poly(ethylene oxide) is the preferred hydrophilic component (column 4, lines 61-61). The diblock polymer may be prepared by using poly(ethylene oxide) that has a methoxy group at one terminal (i.e. methoxy polyethylene oxide) (column 5, lines 61-64). Additionally it is disclosed that the terms PEG and PEO are used interchangeably (column 9, lines 34-35). The block copolymer has a molecular weight in the range of about 1430 to about 6000 Daltons (g/mol). The hydrophilic component is in the range of about 50 to about 70 wt. % based on the total weight of the block copolymer (column 4, lines 55-60). Subsequently, the hydrophobic polymer is present from about 50 to about 30 wt. %.

Suitable hydrophobic drugs which may be incorporated into the block copolymer drug carrier micelle include anti-cancer drugs (column 6, lines 61-66). One particular drug exemplified is Paclitaxel (example 1). It is disclosed that hydrophobic drugs have limited solubilities. In order to achieve the expected therapeutic effect of a drug, it is

usually required that a solubilized form of the drug is administered to a patient (page 1, lines 26-29). It is disclosed that the drug solution obtained may be freeze-dried for long-term storage. The lyophilized composition may be restored to its original solution by using water or an isotonic solution (column 8, lines 69-64). An isotonic solution utilized with the polymer included a phosphate buffer (example 15).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Kim et al. does not indicate that amino acids can be incorporated into the micelle composition. However, this deficiency is cured by Park et al.

Park et al. is directed to pharmaceutical applications of hydrotropic agents. Hydrotropic agents are compounds that solublize poorly water-soluble molecules (paragraph 0033). Examples of hydrotropic materials in the literature include sodium salcylate, sodium gentisate, sodium glycinate, sodium benzoate, lysine, tryptophan, etc. (paragraph 0034).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kim et al. and Park et al. and utilize the amino acids lysine or tryptophan as hydrotropic agents. One of ordinary skill in the art would have been motivated to utilize hydrotropic agents because the micelle compositions are designed to help solubilize poorly soluble drugs such as paclitaxel and hydrotropic agents such as lysine and tryptophan also help to solublize poorly soluble drugs. By including hydrotropic agents

into the micelle compositions as well, one of ordinary skill in the art would expect at least an additive effect in the solubilization of hydrophobic drugs. It would have been obvious to one of ordinary skill in the art to pursue known options within his or her technical grasp, specifically disclosed hydrotropic agents known in the art which include lysine and tryptophan.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Regarding the claimed ranges of claims 27-30, in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]**

Regarding claim 31, Park et al. discloses the same amino acids as claimed. Therefore, the amino acid must have a water-solubility of greater than 2.5 g per 100g water at 25 °C.

Regarding claims 52-53, applicant has indicated that compositions having a moisture content less than 0.5% water have been produced through lyophilization (specification, page 37, lines 27-28). Therefore, since Kim et al. indicates that micelle composition can be lyophilized for long-term storage, this product would have a moisture content less than 0.5%.

Claims 38-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. in view of Park et al. and in further view Patel et al (US Patent No. 6596463).

Applicant Claims

Applicant claims that the composition further comprises MePEG.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Kim et al. and Park et al. are set forth above. Specifically, Kim et al. teaches a micelle composition comprising a diblock copolymer and a hydrophobic drug. Monomers of the polymer include poly (ethylene oxide). Additionally it is disclosed that the terms PEG and PEO are used interchangeably. The compositions are utilized to help solubilize hydrophobic drugs.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Kim et al. does not teach that MePEG can additionally be added. However, this deficiency is cured by Patel et al.

Patel et al. is directed to solid carriers for improved delivery of hydrophobic active ingredients. It is disclosed that solubilizer are additives that increase the solubility of pharmaceutical active ingredients. Suitable solublizers include polyethylene glycols having an average molecular weight of about 200 to about 6000 such as methoxy PEG (MePEG) (column 29, lines 1-35).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kim et al, Park et al., and Patel et al. and utilize MePEG as an additional solubilizer. One of ordinary skill in the art would have been motivated to utilize Me PEG because it is known to increase the solubility of pharmaceutical actives. Therefore, one of ordinary skill in the art would expect that the addition of MePEG would have at least an additive effect in solubilizing pharmaceutical actives.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Regarding the claimed ranges of claims 40-41, in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]**

Claims 43, 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. in view of Park et al. and in further view Saleh et al. (J. Pharm. Sci., 1986).

Applicant Claims

Applicant claims that the composition comprises about 1 to about 5 parts block copolymer per each 1 part additive.

The composition comprises 10-90 (or about 50-80 or about 55-75) parts diblock copolymer, 10-70 (or about 10-40 or about 15-35) parts additive, 1-15 (or about 8, or about 7) parts paclitaxel, and 1-20 (or about 18 or about 11) parts phosphate salt.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Kim et al. and Park et al. are set forth above. Specifically, Kim et al. indicates that hydrophobic drugs can be incorporated into the micelle in an amount from 0.000001 to 30%. The polymer is present from 70 to 99.9 percent (claim 1). It is disclosed that the composition can be restored to solution after freeze-drying by using water or isotonic solution. Isotonic solution utilized with the polymer included a phosphate buffer.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Kim et al. does not teach the amount of additive that can be added to the micelle composition. However, this deficiency is cured by Saleh et al.

Saleh et al. is directed various solubilization by various hydrotropic salts. It is disclosed that the concentrations of the hydrotropic agents is from 0 to 30%. The salts include sodium salcylate, sodium gentisate, sodium glycinate, and sodium benzoate (table 1).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kim et al., Park et al., and Saleh et al. and utilize a hydrotropic agent in an amount up to 30 percent. One of ordinary skill in the art would have been motivated to

utilize these percentages because Saleh et al. discloses that these are suitable percentages for hydrotropic agents.

It would have been obvious to one of ordinary skill in the art to adjust the amount of polymer depending on the amount of hydrotropic agent added. It is within the skill of an artisan to optimize the ratio of hydrotropic agent to polymer to determine the optimal amount to increase the solubility of the hydrophobic drug.

It would have been obvious to one of ordinary skill in the art at the time of the invention to engage in route experimentation to determine optimal or workable ranges that produce expected results.

Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

Claims 54 and 56-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. in view of Park et al. and in further view Kuhn et al. (US Patent No. 6548079).

Applicant Claims

Applicant claims that the composition is sterile and is packaged within a container that maintains the sterility of the composition. The container is glass. The container is plastic. The container allow for sufficient volume of empty space to allow for the addition of water. The package is substantially opaque to UV or visible light. The package is impervious to oxygen.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Kim et al. and Park et al. are set forth above. Specifically, Kim et al. indicates that micelle composition can be freeze-dried for long-term storage. The composition may be restored to its original solution by using water or an isotonic solution.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Kim et al. does not teach that the composition is sterile or packaged. However, these deficiencies are cured by Kuhn et al.

Kuhn et al. is directed to medicaments used for treating infections in humans or animals. It is disclosed that the compositions can be filled into suitable containers and sterilized in an appropriate matter. The containers can be glass or plastic. The container can contain material protecting the contents against light or against oxygen (column 5, lines 52-58). One particular type exemplified is an injection bottle made of glass and is closed and sterilized (example 8).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kim et al., Park et al., and Kuhn et al. and utilized a suitable container to store the micelle composition. One of ordinary skill in the art would have been motivated to utilize a suitable container because Kim et al. indicates that the compounds can be stored for long-term. One of ordinary skill in the art would have been motivated to select either glass or plastic because these are disclosed as suitable

container types for drug storage. One of ordinary skill in the art would have been motivated to select a container that protects the contents against light or against oxygen to increase the long-term stability of the drug composition.

It would have been obvious to one of ordinary skill in the art to sterilize the container with the composition. One of ordinary skill in the art would have been motivated to sterilize a composition to remove trace bacteria and provide a sterile composition to a consumer. One of ordinary skill in the art would have been motivated to formulate an injection and sterilize it as this is taught by Kuhn et al.

It would have been obvious to one of ordinary skill in the art to allow sufficient volume of empty space to allow for the addition of water. One of ordinary skill in the art would have been motivated to do this because Kim et al. indicates that after the composition is freeze-dried and stored it can be restored to its original solution by using water. Therefore, it would have been obvious to one of ordinary skill in the art to leave enough room to allow for the addition of water to restore the composition into the desired concentration.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 62 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. '805 in view of Park et al. and in further of Kim (US Patent No. 4587124).

Applicant Claims

Applicant claims that the composition further comprises a bactericidal or bacteriostatic compound.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Kim et al. '805 and Park et al. are set forth above. Specifically, Kim et al. '805 is directed to a micelle composition comprising a hydrophobic drug.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Kim et al. does not teach that bactericidal or bacteriostatic compounds can be added. However, this deficiency is cured by Kim '124.

Kim '124 teaches that commonly acceptable pharmaceutical adjuvants include preservatives, antimicrobial agents and the like (column 2, lines 33-35). Antimicrobial agents is a generic group that encompasses bactericidal and baceriostatic compounds.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kim et al. '805, Park et al., and Kim '124 and utilized commonly acceptable pharmaceutical adjuvants such as antimicrobial agents. One of ordinary skill in the art would have been motivated to include antimicrobial agents in the pharmaceutical composition of Kim et al. because Kim '124 discloses that these are commonly acceptable pharmaceutical adjuvants.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. in view of Park et al. and in further of Gotschi (US Patent No. 5036064).

Applicant Claims

Applicant claims that the composition further comprises an antioxidant and a coloring agent.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Kim et al. and Park et al. are set forth above. Specifically, Kim et al. is directed to a micelle composition comprising a hydrophobic drug.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Kim et al. does not teach that the composition further comprises an antioxidant or a coloring agent. However, these deficiencies are cured by Gotschi.

Gotschi teaches that common pharmaceutical adjuvants include preservatives, emulsifiers, sweeteners, colorants, coating agents, antioxidants, etc. (column 14, lines 31-35).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Kim et al., Park et al., and Gotschi and utilized commonly acceptable

pharmaceutical adjuvants such as antioxidants or colorants. One of ordinary skill in the art would have been motivated to include antioxidants or colorants in the pharmaceutical composition of Kim et al. because Gotschi discloses that these are commonly acceptable pharmaceutical adjuvants.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

AF

/Sharmila Gollamudi Landau/

Primary Examiner, Art Unit 1611